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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,648	12/19/2001	Heather J. Belmont	49663 (71758)	2636

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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT.	PAPER NUMBER
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1632

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/024,648	Applicant(s) BELMONT ET AL.	
	Examiner Anne Marie S. Wehbe	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-113 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-113 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 2-8, 30, 31-47, and 112-113, drawn to non-human transgenic animals comprising a human TCR loci and methods of making said animals, classified in classes 800, subclasses 13 and 21.
- II. Claims 9-19, 30-37, and 48-53, drawn to non-human transgenic animals comprising a human TCR loci and human MHC loci and methods of making said animals, classified in class 800, subclasses 13 and 22.
- III. Claims 20-21, 26, 29-37, and 54-57, drawn to non-human transgenic animals comprising a human TCR loci, human MHC loci, and a human co-receptor, and methods of making said animals, classified in class 800, subclasses 13 and 22.
- IV. Claims 20-25, 27-28, and 30-37, drawn to non-human transgenic animals comprising a human TCR loci and a human co-receptor, classified in class 800, subclass 13.
- V. Claims 58-60, drawn to a cell line producing heterologous TCR, classified in class 435, subclass 325.
- VI. Claims 61-65, drawn to nucleic acid encoding a TCR, classified in class 536, subclass 23.1.
- VII. Claims 66-67, drawn to an isolated TCR, classified in class 530, subclass 350.

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- VIII. Claims 68-71, drawn to methods of making immortal cell lines which produce heterologous TCR using transgenic non-human animals, classified in class 435, subclass 436.
- IX. Claims 72-92, drawn to yeast artificial chromosomes comprising human TCR loci, classified in class 435, subclass 320.1.
- X. Claims 93-100, drawn to yeast artificial chromosomes comprising human MHC loci, classified in class 435, subclass 320.1.
- XI. Claims 101-104, drawn to a nucleic acid encoding a co-receptor operably linked to a promoter, classified in class 435, subclass 320.1.
- XII. Claims 105-111, drawn to targeting vectors for homologous recombination, classified in class 435, subclass 463.

Claim 1 links inventions I-IV . The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction

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requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

- 1) Groups I -IV are patentably distinct in that a transgenic animal which comprises a human TCR locus, a transgenic animal which comprises a human TCR locus and a human MHC locus, a transgenic animal which comprises a human TCR locus and a human co-receptor, and a transgenic animal which comprises a human TCR locus, a human MHC locus, and a co-receptor are substantially different in structural, physiological, and functional properties. This is because each of these loci or genes is substantially different in terms of physical, structural, and functional properties. Further, the products of these loci are structurally and functionally different each from the other. In addition, each of these animals is made using different starting materials and techniques. Thus, the transgenic animals of groups I-IV represent patentably distinct inventions.
- 2) Inventions I-IV are patentably distinct from the cell line of invention V in that the cell line can be produced without the use of the transgenic animals of inventions I-IV. The cell line can be produced by transfecting a cell with a vector comprising a heterologous rearranged TCR in vitro. Further, the transgenic animals can be used for purposes other than making a cell line, such as the use of these animals to model human immune responses.
- 3) Inventions I-IV are patentably distinct from the nucleic acid encoding a TCR of invention VI in that the nucleic acids of invention VI comprise a rearranged TCR and thus are not useful in making the transgenic animals of inventions I-IV which comprise a TCR locus. Further, the nucleic acid of invention VI does not require the transgenic animals of inventions I-IV for its

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production since the nucleic acid can be isolated from various cell lines or can be synthesized in vitro.

4) Inventions V and VI are patentably distinct in that the nucleic acid of invention VI can be used for purposes other than making a cell line, such as the use of the nucleic acid to generate probes for in vitro screening assays. Further, the nucleic acid can be produced without the use of the cell line of invention VI in that the nucleic acid can be synthesized.

5) Invention VII is patentably distinct from inventions I-VI in that the isolated TCR polypeptide can be made using either of the transgenic animals or cell lines of inventions I-V, or synthesized in vitro. Thus, the production of TCR polypeptide does not require the use of any of inventions I-VI. Further, the use of the TCR polypeptide does not require the use of any of inventions I-VI in that the polypeptide can be used to generate antibodies in non-transgenic animals, or can be used in various in vitro assays.

6) Invention VIII is patentably distinct from invention I-VII in that immortal cell lines which produce heterologous TCR can be made using other methods than those of invention VIII, such as making the cell lines by transfection of cells in vitro with nucleic acids encoding the rearranged TCR. Further, the transgenic animals of invention I-IV can be used for purposes other than making immortal cell lines, such as the use of the animals as models to study human T cell responses in vivo.

7) Inventions IX-XI are patentably distinct in that a TCR loci, MHC loci, and co-receptor genes are substantially different in terms of physical, structural, and functional properties. Further, the products of these loci are structurally and functionally different each from the other.

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8) Inventions IX-XI are patentably distinct from inventions I-VIII in that the YACs and vectors of inventions IX-XI can be used for purposes other than making transgenic animals or cells.

These vectors can be used to generate probes for in vitro assays. Further, a YAC comprising a TCR locus is unrelated to a vector comprising a rearranged TCR since the genomic locus is unrearranged and does not produce any TCR protein.

9) Invention XII is unrelated to inventions V-XI. A homologous recombination vector for knocking out an endogenous gene or loci does not encode functional TCR or MHC loci or encode a co-receptor or rearranged TCR.

10) Invention XII is patentably distinct from inventions I-IV in that the targeting vectors can be used for other purposes than making a transgenic animal such as the use of the vector to inactivate genes in somatic cells in vitro.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, different classification, and different search requirements, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the

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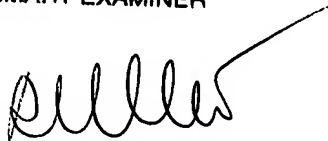
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technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Anne M. Wehbé', with a long, sweeping horizontal line extending to the right.